STUDIES IN THE β-CARBOLINE SERIES

BY

LEON KATZ

B.S., Trinity College, 1944

AN ABSTRACT OF A THESIS

SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN CHEMISTRY
IN THE GRADUATE SCHOOL OF THE
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Introduction

The seeds of the African wild rue, *Peganum harmala*, contain four alkaloids: harmaline, $C_{13}H_{14}ON_2$; harmine, $C_{13}H_{12}ON_2$; harmalol, $C_{12}H_{12}ON_2$; and peganine. The first three alkaloids have been shown to be derivatives of the β-carboline series (1) and to possess physiological activity.

When harman (2-methyl-β-carboline) is nitrated, two isomeric mononitro compounds are isolated by fractional crystallization from pyridine; m. p. 301° and 210°. The orientation of the nitro groups had not been determined.

The object of the present work was the synthesis of compounds closely related to the harmala alkaloids. In particular, it has been concerned with the establishment of the structures of the isomeric nitroharmans and with the development of improved preparations of tryptamine and derivatives of tryptamine which can be converted to β-carbolines.

Discussion of Results

7-Bromoharman has been synthesized unequivocally from *m*-toluidine through the following intermediates, according to a modification of a procedure by Robson (2):

2-Nitro-5-aminotoluene
2-Nitro-5-bromotoluene
Potassium Salt of Ethyl 2-Nitro-5-bromophenylpyruvate
5-Bromoindole-2-carboxylic Acid
5-Bromoindole
3-Dimethylaminomethyl-5-bromoindole
5-Bromotryptophane
2-Methyl-2,3,4,5-tetrahydro-4-carboxy-7-bromo-β-carboline
2-Methyl-7-bromo-β-carboline (7-Bromoharman).

The 7-bromoharman was purified as the monopicrate and compared with the bromoharman picrate prepared from the high-melting nitroharman. The melting points were identical, 291-293°, and a mixed melting point showed no depression; 291-293°. To complete the proof of identity, the infra-red absorption spectra were determined. These absorption curves were identical in every detail, whereas the curves of the two isomeric nitro compounds, run for comparison, were plainly dissimilar.

2-Homoanisyl-2,3,4,5-tetrahydro-4-carboxy-β-carboline has been prepared by the reaction of *dl*-tryptophane with homoanisaldehyde bisulfite and has been submitted for testing.

Harman-7-arsonic acid, of interest as a possible new trypanocidal agent, has been prepared from 7-aminoharman by a modified Bart procedure. This arsenical has been submitted for testing.

The alkylation of 1-nitropropane and 2-nitropropane with the Mannich base of indole (gramine) has been accomplished. The resulting nitro compounds have been converted to the amines, α-ethyltryptamine and α,α-dimethyltryptamine, which have been submitted for testing. The alkylation of nitroethane with gramine resulted in a poor yield, and the alkylation of nitromethane with gramine was unsuccessful. From the latter reaction a small quantity of diindolylnitromethane was isolated.

N-Benzoyl-α-ethyltryptamine and N-benzoyl-α,α-dimethyltryptamine have been prepared and the benzoyl derivative of the former has been cyclodehydrated to 2-phenyl-4-ethyl-4,5-dihydro-β-carboline.

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VITA

The author was born in Springfield, Massachusetts, on August 27, 1921. He received his elementary education in the public schools of Hartford, Connecticut, graduating from high school in June, 1939. In September, 1940, he entered Trinity College, from which he received the degree of Bachelor of Science in Chemistry in 1944. In the fall of the same year he entered the University of Illinois. From September, 1945, to June, 1947, he was a University of Illinois Fellow.

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